

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

RECEIVED
JAN 02 2001
File Information Unit

In re Application of	
<i>Bendig</i>	
Application Number	Filed
08/186269	11/21/98
Group Art Unit	Examiner

Paper No. #19Assistant Commissioner for Patents
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

(A) referred to in United States Patent Number 5840299, column _____,

(B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____, on page _____ of paper number _____,

(C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____, or

(D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

Nancy Perry
Signature

Nancy Perry
Typed or printed name

1/2/01
Date

FOR PTO USE ONLY	
Approved by: <i>GL</i>	
File <u>File</u> (initials) Unit	
Unit: _____	

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. The time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



US005840299A

United States Patent [19]

Bendig et al.

[11] Patent Number: 5,840,299

[45] Date of Patent: Nov. 24, 1998

[54] **HUMANIZED ANTIBODIES AGAINST LEUKOCYTE ADHESION MOLECULE VLA-4**

[75] Inventors: **Mary M. Bendig**, London; **Olivier J. Léger**, Hertfordshire; **José Saldanha**, Enfield Middlesex; **S. Tarren Jones**, Radlett, all of United Kingdom; **Ted A. Yednock**, Fairfax, Calif.

[73] Assignee: **Athena Neurosciences, Inc.**, South San Francisco, Calif.

[21] Appl. No.: 561,521

[22] Filed: Nov. 21, 1995

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 186,269, which is a continuation-in-part of PCT/US95/01219 Jan. 25, 1995, abandoned.

[51] Int. Cl. 6 A61K 39/395; C07K 16/28; C12P 21/08; C12N 15/13

[52] U.S. Cl. 424/133.1; 424/130.1; 424/141.1; 424/143.1; 424/144.1; 424/153.1; 424/154.1; 424/173.1; 435/7.1; 435/7.2; 435/7.21; 435/7.24; 435/69.6; 435/172.3; 435/251.3; 435/320.1; 530/387.3; 530/388.73; 530/388.75; 530/388.22; 536/23.53

[58] Field of Search 424/130.1. 133.1. 424/141.1. 143.1. 144.1. 153.1. 154.1. 173.1; 435/69.6. 172.3. 252.3. 320.1. 7.1. 7.2. 7.21. 7.24; 536/23.4. 23.5. 23.53; 530/387.1. 387.3. 388.2. 388.22. 388.7. 388.73. 388.75

[56] References Cited

U.S. PATENT DOCUMENTS

5,260,210 11/1993 Rubin et al. 435/240.23
5,530,101 6/1996 Queen et al. 530/387.3

FOREIGN PATENT DOCUMENTS

239400 9/1987 European Pat. Off. C12N 15/00
330506 8/1989 European Pat. Off. C07K 15/06
XWO 90/07861 7/1990 WIPO C12P 21/00
XWO 91/03252 3/1991 WIPO A61K 37/10
91/05038 4/1991 WIPO C12N 5/06
XWO 93/15764 8/1993 WIPO A61K 39/395

OTHER PUBLICATIONS

XLisak et al. J. Neurol. Sciences 62: 281-293 (1983).
XTeitelbaum et al. PNAS 89: 137-141 (1992).
XWeiner et al. Science 259: 1321-1324 (1993).
XRacke et al. J. Neuroimmunol. 46: 175-184 (1993).
XKarussis et al PNAS 90: 6400-6404 (1993).

X Cannella et al. Ann Neurol. 37: 424-435 (1995).
X Washington et al. Ann Neurol 35: 89-97 (1994).
X Dore-Duffy et al. in *Frontiers in Cerebral Vascular Biology: Transport and its Regulation* (eds) Dreues and Betz Plenum Press Ny 1993 pp. 243-248.
Monshizadegan et al., "VLA-4-dependent adhesion activities of U937 cells and guinea pig bronchoalveolar lavage leukocytes", 1993, *Agents Actions* 39, pp. C177-C179.
Kettleborough et al., "Humanization of a mouse monoclonal antibody by CDR-grafting the importance of framework residues on loop conformation", 1991, *Protein Engineering*, vol. 4, No. 7, pp. 773-783.
Yednock et al. "Prevention of experimental autoimmune encephalomyelitis by antibodies against $\alpha 4\beta 1$ integrin", 1991, *Letters to Nature*, vol. 356, pp. 63-66.
W. J. Harris and S. Emery, "Therapeutic antibodies—the coming of age", 1993, *Tibtech*, vol. 11, pp. 42-45.
S. C. Emery and J. R. Adair, "Humanised monoclonal antibodies for therapeutic applications", 1994, *Exp. Opin. Invest. Drugs*, vol. 3, pp. 241-251.
S. M. Edgington, "How Sweet It Is: Selectin-Mediating Drugs", 1992, *Bio/Technology*, vol. 10, pp. 383-389.
Elices et al., "VCAM-1 on Activated Endothelium Interacts with the Leukocyte Integrin VLA-4 at a Site Distinct from the VLA-4/Fibronectin Binding Site", 1990, *Cell*, vol. 60, pp. 577-584.
Dijkstra et al., "Multiple sclerosis: some possible therapeutic opportunities", 1993, *Tips Reviews*, vol. 14, pp. 124-129.
A. Mountain and J.R. Adair, "Engineering Antibodies for Therapy", 1992, *Biotech Genetic Engineering Reviews*, vol. 10, pp. 10-13.
P.A. Ward and M.S. Mulligan, "Blocking of adhesion molecules in vivo as anti-inflammatory therapy", 1994, *Therapeutic Immunol*, vol. 10, pp. 165-171.
L. K. Jolliffe, "Humanized Antibodies: Enhancing Therapeutic Utility Through Antibody Engineering", 1993, *Intern Rev Immunol*, vol. 10, pp. 241-250.
X Albeda Faseb J. 8: 504-512 (1994).
X Kahan Curr Opin Immunology 4: 553-560 (1992).
X Natanson et al. Ann Intern Med. 120: 771-783 (1994).
X Dalakas Ann. Neurol. 37(51): 52-513 (1995).
X Paul (ed) *Fundamental Immunology* Raven Press NY 1993 p. 242 only.

Primary Examiner—Lila Feisee

Assistant Examiner—Phillip Gambel

Attorney, Agent, or Firm—Townsend & Townsend & Crew LLP

[57]

ABSTRACT

The invention provides humanized immunoglobulins that specifically bind to the VLA-4 ligand, and methods of treatment using the same. The methods are particularly useful for treatment of multiple sclerosis.

29 Claims, 16 Drawing Sheets